

IN THE CLAIMS:

Amend the claims as follows.

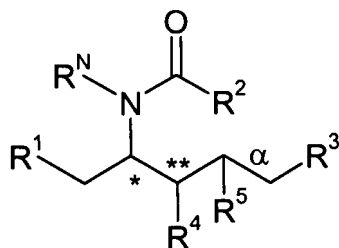
Claims 1-91. (Canceled)

92. (New) A pharmaceutical formulation comprising:

(i) a drug; and

(ii) a short-chain sphingolipid selected from compounds of

the following formula:



wherein:

R¹ is independently:

an O-linked saccharide group; or

an O-linked polyhydric alcohol group;

or:

R¹ is independently:

an O-linked (optionally N-(C₁₋₄alkyl)-substituted

amino)-C₁₋₆alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)-C₁₋₆alkyl-
phosphate group;

R² is independently C₃₋₉alkyl,

and is independently unsubstituted or substituted;

R³ is independently C₇₋₁₉alkyl,

and is independently unsubstituted or substituted;

R⁴ is independently -H, -OH, or -O-C₁₋₄alkyl;

R^N is independently -H or C₁₋₄alkyl;

the bond marked with an alpha (α) is independently a
single bond or a double bond;

if the bond marked with an alpha (α) is a double bond, then
R⁵ is -H;

if the bond marked with an alpha (α) is a single bond, then
R⁵ is -H or -OH;

the carbon atom marked (*) is independently in an R-
configuration or an S-configuration;

the carbon atom marked (**) is independently in an R-configuration or an S-configuration;

and pharmaceutically acceptable salts, solvates, esters, and ethers thereof.

93. (New) A pharmaceutical formulation according to claim 92, wherein said drug is an amphiphilic drug.

94. (New) A pharmaceutical formulation according to claim 92, wherein said drug is an anthracycline.

95. (New) A pharmaceutical formulation according to claim 92, wherein said drug is selected from: doxorubicin, idarubicin, epirubicin, aclarubicin, mitrozantrone, and daunorubicin, and salts thereof.

96. (New) A pharmaceutical formulation according to claim 92, wherein said drug is doxorubicin or doxorubicin hydrochloride.

97. (New) A pharmaceutical formulation according to claim 92, wherein said drug is an alkaloid.

98. (New) A pharmaceutical formulation according to claim 92, wherein said drug is selected from: topotecan and camptothecin.

99. (New) A pharmaceutical formulation according to claim 92, wherein R^2 is independently linear.

100. (New) A pharmaceutical formulation according to claim 92, wherein R^2 is independently linear; and has from 0 to 3 carbon-carbon double bonds.

101. (New) A pharmaceutical formulation according to claim 92, wherein R^2 is independently unsubstituted or substituted with from 1 to 3 substituents selected from C_{1-4} alkyl, -OH, C_{1-4} alkoxy, -C(=O)OH, and -C(=O)O- C_{1-4} alkyl.

102. (New) A pharmaceutical formulation according to claim 92, wherein R^2 is independently $-(CH_2)_nCH_3$, wherein n is an integer from 4 to 8.

103. (New) A pharmaceutical formulation according to claim 92, wherein R^2 is independently $-(CH_2)_nCH_3$, wherein n is an integer from 6 to 8.

104. (New) A pharmaceutical formulation according to claim 92, wherein R^2 is independently $-(CH_2)_6CH_3$.

105. (New) A pharmaceutical formulation according to claim 92, wherein the bond marked alpha is independently a double bond and R^5 is -H.

106. (New) A pharmaceutical formulation according to claim 92, wherein the bond marked alpha is independently a single bond; and R^5 is -H.

107. (New) A pharmaceutical formulation according to claim 92, wherein the bond marked alpha is independently a single bond; and R⁵ is -OH.

108. (New) A pharmaceutical formulation according to claim 92, wherein R³ is independently linear.

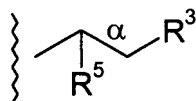
109. (New) A pharmaceutical formulation according to claim 92, wherein R³ is independently linear; and has from 0 to 3 carbon-carbon double bonds.

110. (New) A pharmaceutical formulation according to claim 92, wherein R³ is independently unsubstituted or substituted with from 1 to 3 substituents selected from C₁₋₄alkyl, -OH, C₁₋₄alkoxy.

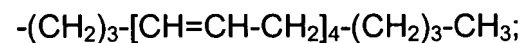
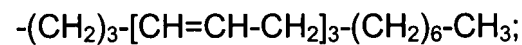
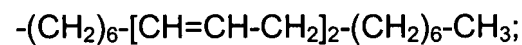
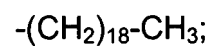
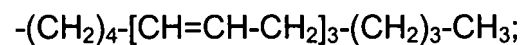
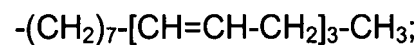
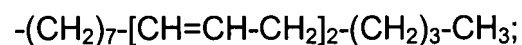
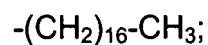
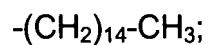
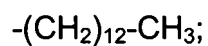
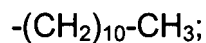
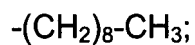
111. (New) A pharmaceutical formulation according to claim 92, wherein R³ is independently -(CH₂)_nCH₃, wherein n is an integer from 8 to 16.

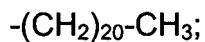
112. (New) A pharmaceutical formulation according to claim 92, wherein R³ is independently -(CH₂)₁₂CH₃.

113. (New) A pharmaceutical formulation according to claim 92, wherein the moiety:



is selected from the following:





analogues wherein the left-most $-(\text{CH}_2)_2-$ is replaced
with $-\text{CH}=\text{CH}-$; and

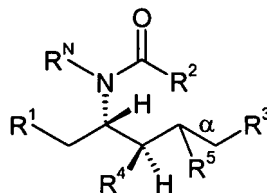
analogues wherein the left-most $-(\text{CH}_2)-$ is replaced with
 $-\text{CH}(\text{OH})-$.

114. (New) A pharmaceutical formulation according to claim 92,
wherein R^4 is independently $-\text{H}$, $-\text{OH}$, $-\text{OMe}$, $-\text{OEt}$, $-\text{O}(\text{iPr})$, $-\text{O}(\text{nPr})$,
 $-\text{O}(\text{nBu})$, $-\text{O}(\text{iBu})$, $-\text{O}(\text{sBu})$, or $-\text{O}(\text{tBu})$.

115. (New) A pharmaceutical formulation according to claim 92,
wherein R^4 is independently $-\text{OH}$.

116. (New) A pharmaceutical formulation according to claim 92,
wherein R^{N} is independently $-\text{H}$, $-\text{Me}$, or $-\text{Et}$.

117. (New) A pharmaceutical formulation according to claim 92,
wherein the carbon atoms marked (*) and (**) have a configuration as
shown in the following formula:



118. (New) A pharmaceutical formulation according to claim 92, wherein R¹ is independently an O-linked saccharide group.

119. (New) A pharmaceutical formulation according to claim 92, wherein R¹ is independently an O-linked mono-, di-, or tri-saccharide group.

120. (New) A pharmaceutical formulation according to claim 92, wherein R¹ is formed from a group or groups selected from:

arabinose, lyxose, ribose, or xylose;

allose, altrose, glucose, mannose, gulose, idose,
galactose, or talose;

and derivatives thereof.

121. (New) A pharmaceutical formulation according to claim 92, wherein R¹ is independently an O-linked mono-, di-, or tri-saccharide group derived from:

arabinose, lyxose, ribose, or xylose;

allose, altrose, glucose, mannose, gulose, idose,
galactose, or talose;

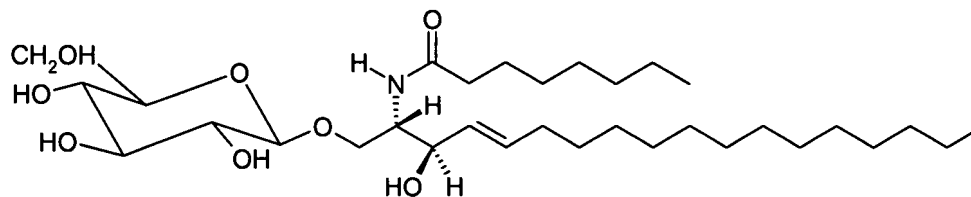
sucrose, maltose, lactose, cellobiose, or galabiose;

globotriaose, isoglobotriaose, mucotriaose,
lactotriaose, neolactotriaose gangliotriaose, galactriaose, mollutriaose, or
antrotriaose;

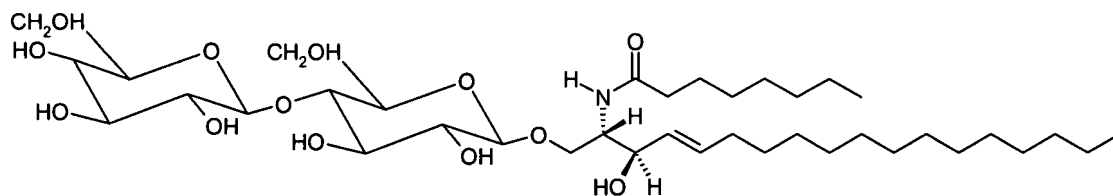
or a derivative thereof.

122. (New) A pharmaceutical formulation according to claim 120,
wherein said saccharide group derivatives are selected from deoxy, di-
deoxy, di-deoxy-di-dehydro, methoxy (-OMe), acetoxy (-OC(=O)Me),
carboxylic acid (-C(=O)OH), sulfuric acid (-OSO₃H), amino-deoxy (e.g., -
NH₂), N-acetyl-amino-deoxy (e.g., -NHC(=O)Me), or N-sulfo-amino-deoxy
(e.g., -NHS(O)₂OH) derivatives.

123. (New) A pharmaceutical formulation according to claim 92,
wherein said short-chain sphingolipid has the following formula
(C₈-GlcCer):



124. (New) A pharmaceutical formulation according to claim 92,
wherein said short-chain sphingolipid has the following formula:



125. (New) A pharmaceutical formulation according to claim 92,
wherein R¹ is independently an O-linked polyhydric alcohol group.

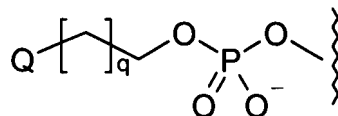
126. (New) A pharmaceutical formulation according to claim 125,
wherein R¹ is formed from groups selected from: ethanediol (glycol),
propanediol, butanediol, glycerol, and erythritol.

127. (New) A pharmaceutical formulation according to claim 92,
wherein R¹ is independently:

an O-linked (optionally N-(C₁₋₄alkyl)-substituted amino)-
C₁₋₆alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)-C₁₋₆alkyl-
phosphate group.

128. (New) A pharmaceutical formulation according to claim 92,
wherein R¹ is independently:



wherein:

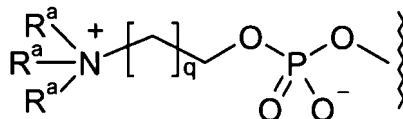
q is independently an integer from 0 to 5;

Q is independently: -NH₂, -NHR^a, -NR^a₂, or -NR^a₃⁺; or:

Q is independently a polyhydric alcohol group, linked via an
oxygen atom;

each R^a is independently linear or branched saturated
C₁₋₄alkyl.

129. (New) A pharmaceutical formulation according to claim 92,
wherein R¹ is independently:

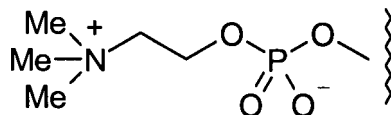


wherein:

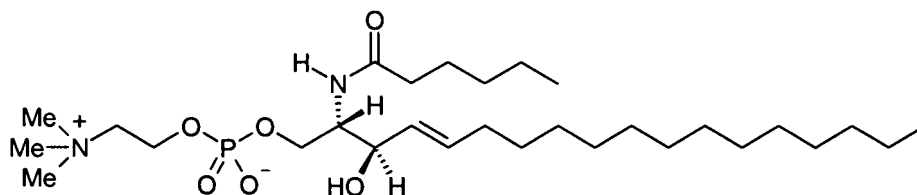
q is independently an integer from 0 to 5; and

each R^a is independently a C₁₋₄alkyl group.

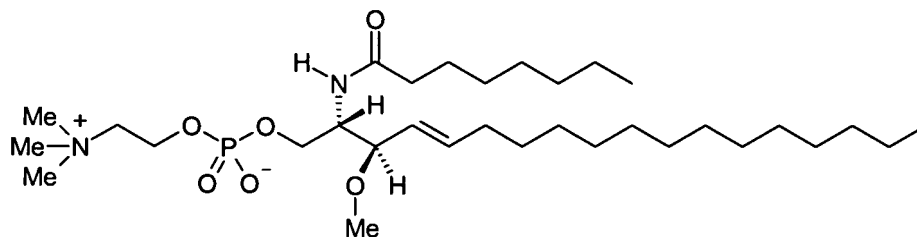
130. (New) A pharmaceutical formulation according to claim 92,
wherein R¹ is independently:



131. (New) A pharmaceutical formulation according to claim 92,
wherein said short-chain sphingolipid has the following formula ("C₆-SM"):



132. (New) A pharmaceutical formulation according to claim 92,
wherein said short-chain sphingolipid has the following formula ("3-O-methyl-C₈-SM"):



133. (New) A pharmaceutical formulation according to claim 128,
wherein Q is independently a polyhydric alcohol group, linked via an
oxygen atom.

134. (New) A pharmaceutical formulation according to claim 133, wherein Q is formed from a group selected from: ethanediol (glycol), propanediol, butanediol, glycerol, and erythritol.

135. (New) A pharmaceutical formulation according to claim 92, wherein said pharmaceutical formulation is suitable for parenteral administration.

136. (New) A pharmaceutical formulation according to claim 92, wherein the pharmaceutical formulation is a liposomal pharmaceutical formulation.

137. (New) A liposomal pharmaceutical formulation according to claim 136, wherein the liposomes of the liposomal pharmaceutical formulation are prepared using a mixture of lipids comprising, at least, vesicle-forming lipids and said short-chain sphingolipid.

138. (New) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises phospholipids and said short-chain sphingolipid.

139. (New) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises phospholipids, cholesterol, and said short-chain sphingolipid.

140. (New) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises phosphatidylcholines, cholesterol, and said short-chain sphingolipid.

141. (New) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises fully hydrogenated soy phosphatidylcholine (HSPC), cholesterol, and said short-chain sphingolipid.

142. (New) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises dipalmitoyl-phosphatidylcholine (DPPC), cholesterol, and said short-chain sphingolipid.

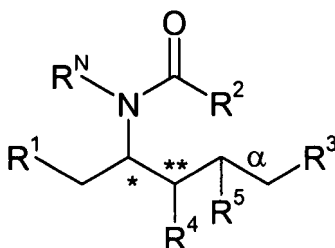
143. (New) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids additionally comprises a vesicle-forming lipid which is derivatized with a polymer chain.

144. (New) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids additionally comprises a phosphatidylethanolamine (PE) which is derivatized with polyethyleneglycol (PEG).

145. (New) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids additionally comprises N-

(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt (MPEG2000-DSPE).

146. (New) Caelyx® or Doxil® liposomes post-inserted with a short-chain sphingolipid selected from compounds of the following formula:



wherein:

R¹ is independently:

an O-linked saccharide group; or

an O-linked polyhydric alcohol group;

or:

R¹ is independently:

an O-linked (optionally N-(C₁₋₄alkyl)-substituted amino)-C₁₋₆alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)-C₁₋₆alkyl-phosphate group;

R^2 is independently C_{3-9} alkyl,

and is independently unsubstituted or
substituted;

R^3 is independently C_{7-19} alkyl,

and is independently unsubstituted or
substituted;

R^4 is independently -H, -OH, or -O- C_{1-4} alkyl;

R^N is independently -H or C_{1-4} alkyl;

the bond marked with an alpha (α) is independently a
single bond or a double bond;

if the bond marked with an alpha (α) is a double bond,
then R^5 is -H;

if the bond marked with an alpha (α) is a single bond,
then R^5 is -H or -OH;

the carbon atom marked (*) is independently in an R-
configuration or an S-configuration;

the carbon atom marked (**) is independently in an R-
configuration or an S-configuration;

and pharmaceutically acceptable salts, solvates, esters, and ethers thereof.

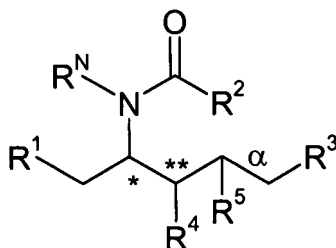
147. (New) A method of making a pharmaceutical formulation according to claim 92, comprising the step of admixing said drug and said short-chain sphingolipid.

148. (New) A method of treating a proliferative condition comprising administering to a patient in need of treatment an effective amount of a pharmaceutical formulation according to claim 92.

149. (New) A method according to claim 148, wherein said proliferative condition is cancer.

150. (New) A method according to claim 148, wherein the drug is doxorubicin or a salt thereof; and the proliferative condition is a proliferative condition that is treated by doxorubicin or a salt thereof.

151. (New) A method of increasing the bioavailability and/or cellular uptake of a drug, which method includes the step of co-administering said drug with a short-chain sphingolipid selected from compounds of the following formula:



wherein:

R^1 is independently:

an O-linked saccharide group; or

an O-linked polyhydric alcohol group;

or:

R^1 is independently:

an O-linked (optionally N-(C₁₋₄alkyl)-substituted amino)-C₁₋₆alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)-C₁₋₆alkyl-phosphate group;

R^2 is independently C₃₋₉alkyl,

and is independently unsubstituted or substituted;

R^3 is independently C₇₋₁₉alkyl,

and is independently unsubstituted or
substituted;

R^4 is independently -H, -OH, or -O-C₁₋₄alkyl;

R^N is independently -H or C₁₋₄alkyl;

the bond marked with an alpha (α) is independently a
single bond or a double bond;

if the bond marked with an alpha (α) is a double bond,
then R^5 is -H;

if the bond marked with an alpha (α) is a single bond,
then R^5 is -H or -OH;

the carbon atom marked (*) is independently in an R-
configuration or an S-configuration;

the carbon atom marked (**) is independently in an R-
configuration or an S-configuration;

and pharmaceutically acceptable salts, solvates,
esters, and ethers thereof.